REMARKS

Reconsideration of the instant application in view of the present amendment and the following comments is respectfully requested. Claims 1-21, 43-59 and 64-96 are pending in the application and claims 1, 19-21, 43, 64, 80 and 81 have been amended. Support for the amendments may be found in the specification and drawings, for example, at page 64, line 26 through page 66, line 2; at page 17, lines 1-16 and in Figure 4. No new matter has been added to the application.

REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-21, 43-59 and 64-96 stand rejected under 35 U.S.C. §112, second paragraph, for alleged indefiniteness. Specifically, the PTO is unclear regarding to what step or steps the recitation "without repeating" refers.

Applicants respectfully traverse these grounds for rejection and submit that the meanings of the instant claims are clear and that the specification fully complies with the requirements of 35 U.S.C. §112, Second Paragraph. The present invention is directed in pertinent part to the recited methods of identifying an agent, comprising the recited steps of contacting, determining and comparing. In particular, and for reasons discussed in detail in Applicants' response previously made of record in the response filed on August 6, 2003, the recited step of determining comprises, in pertinent part, determining "under conditions that permit identification of (i) mitochondrial calcium uniporter activity, wherein a decrease over time in the signal that is proportional to the level of calcium in the cytosol indicates mitochondrial calcium uniporter activity, and (ii) mitochondrial uncoupler or respiratory inhibitor activity, wherein an increase over time in the signal that is proportional to the level of calcium in the cytosol without repeating step (a) indicates mitochondrial uncoupler or respiratory activity". (emphasis added)

Accordingly, Applicants are somewhat puzzled by the PTO's confusion concerning to what step or steps the recitation "without repeating" refers, given that even prior to the present amendment the instant claims recited in pertinent part "without repeating (a)" as a

clear and unambiguous reference to *step* (a) of each claim. (See, *e.g.*, response filed on August 6, 2003, at page 19, lines 24-28). Nevertheless, without acquiescence in the rejection, to make explicit what was implicit, and solely for purposes of advancing the prosecution of the present application, according to the amendment submitted herewith the instant claims now recite in pertinent part "without repeating step (a)". The step to which "without repeating" refers is clearly step (a), such that the rejection for indefiniteness has been overcome.

Applicants respectfully submit that the application therefore satisfies all requirements of 35 U.S.C. §112, second paragraph, and wish to point out further that the pertinent portion of recited step (b) in the presently amended claims is directed to

"detecting . . . the signal . . . under conditions that permit identification of . . . (ii) mitochondrial uncoupler or respiratory inhibitor activity, wherein an increase over time in the signal that is proportional to the level of calcium in the cytosol without repeating step (a) indicates mitochondrial uncoupler or respiratory activity". (emphasis added).

Accordingly, and as discussed in greater detail in the papers Applicants have previously made of record, the specification describes and the claims clearly and distinctly point out the <u>conditions</u> that are present when the invention is practiced, but actually repeating step (a) is neither precluded nor required in order to practice the method of claims 1, 19-21, 43, 64, 80 or 81. In particular, as disclosed in the specification and recited in the claims, detecting the signal at a plurality of time points without repeating step (a) can permit identification of mitochondrial uncoupler or respiratory inhibitor activity if the signal increases over time, when conditions that permit such identification according to the method described by the instant application are present.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. §112, Second Paragraph, be withdrawn.

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to Deposit Account No. 19-1090.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,
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